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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,626	01/10/2005	Manuel Rosa-Calatrava	017753-200	9366

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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
12/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,626	ROSA-CALATRAVA ET AL.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4, 8-43* is/are pending in the application.

4a) Of the above claim(s) *2-4,8-15,17,18,28,35-39,42 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,16,19-27,29-34,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office action.

2. Claims 5-7 have been cancelled. Claims 2-4, 8-15, 17, 18, 28, 35-39, 42, and 43 have been withdrawn.

Claims 1, 16, 19-27, 29-34, 40, and 41 are under examination.

Response to Arguments

Claim Rejections - 35 USC § 102

3. The rejection of claims 1, 16, 19-27, 30-34, 40, and 41 under 35 U.S.C. 102(e) as being anticipated by Wickham et al. (U.S. Patent No. 6,455,314) is withdrawn in response to Applicant's amendments to the claims filed on 10/10/2007.

Claim Rejections - 35 USC § 103

4. The rejection of claims 1, 16, 19-27, 29-34, 40, and 41 under 35 U.S.C. 103(a) as being unpatentable over Wickham et al., in view of Seth et al. (U.S. Patent No 5,928,944) is withdrawn in response to Applicant's amendments to the claims filed on 10/10/2007.

New Rejections

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 16, 19-27, 29-34, 40, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wickham et al. (U.S. Patent No. 6,455,314, of record), in view of both Wallach et al. (WO 97/37016) and Seth et al. (U.S. Patent No 5,928,944, of record).

Wickham et al. teach **(i)** a mutated adenoviral fiber protein, wherein the adenoviral fiber protein comprises at least one mutation affecting the lysine at position 506, the histidine at position 508, and the serine at position 555 of the wild type adenoviral fiber protein set forth by SEQ ID NO: 1, and wherein the affected amino acid residues are involved in the interaction with cellular receptors containing glycosaminoglycans or sialic acid (claim 1), **(ii)** a trimer comprising the mutated adenoviral fiber protein (claim 16), **(iii)** a DNA encoding the mutated adenoviral fiber protein (claim 19), and **(iv)** an adenoviral particle wherein wild type adenoviral fiber is replaced with the mutated adenoviral fiber trimer above, wherein the adenoviral particle comprises a penton base having mutations affecting a native RGD sequence, wherein the adenoviral particle exhibits reduced ability to interact with the native receptors, wherein the adenoviral particle can further include non-native ligands that can bind cellular receptors and wherein the non-native ligands can be incorporated into the fiber at any location that exposes the ligand, such as the terminus of the fiber protein (i.e.,

genetically coupled to a viral polypeptide exposes at the surface, wherein one of the locations could be the C-terminus) (claims 20-27) (Abstract, column 7, lines 10-18 and 37-67, column 9, lines 20-67, column 10, lines 1-67, column 12, lines 29-31, column 17, lines 20-27, Table 1; see also the attached sequence alignment). Wickham et al. teach that the adenoviral particle can comprise adenoviral genome and it can be replication defective (claims 30 and 31), that the adenoviral particle can be used deliver genes to target cells, wherein the genes are operably linked to tissue-specific promoters and wherein the target cells have surface receptors capable of binding the ligand exposed on the surface of the adenoviral particle (claims 32-34) (column 13, lines 7-67, column 14, lines 25-30). Wickham et al. also teach a composition comprising the adenoviral particle and a pharmaceutically acceptable carrier (claim 40), wherein the adenoviral particle is conjugated to lipid derivatives of PEG (claim 41) (column 1, lines 42-50, column 14 bridging column 15).

Although Wickham et al. teach mutations affecting the lysine at position 506, the histidine at position 508, and the serine at position 555 of the wild type adenoviral fiber protein set forth by SEQ ID NO: 1, they do not specifically teach substituting the lysine in the position 506 by glutamine, the histidine in position 508 by lysine, or the serine in position 555 by lysine (claim 1). However, this is not innovative over the prior art, which teaches obtaining protein analogs by using conservative substitutions such as replacing lysine with glutamine or histidine with lysine (see for example, Wallach et al. teach, p. 23, Table I A, p. 24, Table I B). Therefore, it would have been obvious to one of skill in the art, at the time the invention was made, to modify the adenoviral fiber protein at one

the positions taught by Wickham et al., by using the conservative mutations taught by Wallach et al., with a reasonable expectation of success. It is noted that, by doing such, one of skill in the art would have obtained a modified fiber proteins having glutamine at position 506 or lysine at position 508 (claim 1). One of skill in the art would have been motivated to use such conservative mutations in order to obtain the desired binding activity, without altering the biological activity characteristic of an adenoviral fiber protein. One of skill in the art would have been expected to have a reasonable expectation of success in doing such because Wallach et al. teach that only routine experimentation is required to determine which substitution(s) results in the desired property (p. 22, lines 7-13).

Wickham et al. and Wallach et al. do not teach the adenoviral particle being an empty capsid (claim 29). Seth et al. teach a method of adenoviral-mediated transfection, wherein the adenovirus is an empty capsid (Abstract, column 5, lines 22-35, column 8, lines 54-58). It would have been obvious to one of skill in the art, at the time the invention was made, to obtain an empty adenovial capsid comprising the mutated fiber protein of Wickham et al. and Wallach et al., with a reasonable expectation of success. One of skill in the art would have been motivated to obtain such capsids to use them according to the teachings of Seth et al., who disclose that such capsids are efficient in mediating transfection without destroying the host cell (column 8, lines 24-58). One of skill in the art would have been expected to have a reasonable expectation of success in making empty capsid because the art teaches that such capsids can be successfully obtained.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD